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EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
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15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/736,960	Applicant(s) LU ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *5,16-29 and 31-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-15,30 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-40* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s).
4) ☒ Interview Summary (PTO-413) Paper No(s). *15*
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 21 February 2003 (Paper No. 14) has been entered in full. Claims 1-2, 4, 9, 13, and 30 are amended and claims 38-40 are added. It is noted that Applicant has requested a corrected filing receipt. Such will be mailed after this response.

This application contains claims 5, 16-29, and 31-37 drawn to an invention nonelected without traverse in Paper No. 10 (19 March 2002). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 6-15, 30, and 38-40 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to the priority as set forth at pg 2-3 of the previous Office Action (Paper No. 12, 14 August 2002) is *withdrawn* in view of the amended specification and newly submitted Application Data Sheet (Paper No. 14, 21 February 2003).

2. The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (Paper No. 14, 21 February 2003) has been considered and is found persuasive. Therefore, the requirements set forth in the Office Action of 14 August 2002 (Paper No. 12) are *withdrawn*.

3. The objections to the specification as set forth at pg 3-4 of the previous Office Action (Paper No. 12, 14 August 2002) are *withdrawn in part* in view of the amended specification (Paper No. 14, 21 February 2003). Please see section on Specification, below.

4. The objection to claim 1 as set forth at pg 4 of the previous Office Action (Paper No. 12, 14 August 2002) is *withdrawn* in view of the amended claim (Paper No. 14, 21 February 2003).

5. The rejection of claim 3 under 35 U.S.C. § 112, first paragraph (deposit rules) as set forth at pg 17-18 of the previous Office Action (Paper No. 12, 14 August 2002) is *withdrawn* in view of the statement of availability and receipt from ATCC for the deposit (Paper No. 14, 21 February 2003).

6. The rejection of claim 30 under 35 U.S.C. § 112, first paragraph (enablement) as set forth at pg 13-14 of the previous Office Action (Paper No. 12, 14 August 2002) for recitation of the term "pharmaceutical" is *withdrawn in part* in view of the amended claim (Paper No. 14, 21 February 2003).

7. The rejection of claims 1, 6-11, 14-15, and 30 under 35 U.S.C. § 103(a) as set forth at pg 19-20 of the previous Office Action (Paper No. 12, 14 August 2002) is *withdrawn* in view of Applicant's persuasive arguments (Paper No. 14, 21 February 2003). However, it is noted that nucleotides 3199-7215 of SEQ ID NO: 1 of the instant application correspond to nucleotides 7-4026 of provisional application 60/196,528.

Specification

8. The objection to the disclosure regarding the referencing of patent applications is

Claim Rejections - 35 USC § 101 and § 112, first paragraph

9. Claims 1-4, 6-15, 30, and 38-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth for originally filed claims 1-4, 6-15, and 30 at pg 4-9 of the previous Office Action (Paper No. 12, 14 August 2002).

The claims are directed to an isolated Cadherin-like asymmetry protein-5 (CLASP-5) polynucleotide wherein the polynucleotide encodes at least 20 contiguous amino acids of SEQ ID NO: 2 or a biologically active variant or an allelic variant thereof. The claims also recite an isolated CLASP-5 polynucleotide comprising a nucleotide sequence that has at least 90% identity to SEQ ID NO: 1. The claims recite an isolated polynucleotide comprising at least 50 contiguous nucleotides of SEQ ID NO: 1. The claims recite a polynucleotide that the hybridizes to SEQ ID NO: 1 under conditions of high stringency and a polynucleotide that encodes a polypeptide having 95% or more sequence identity with SEQ ID NO: 2. The claims also recite an expression vector comprising the polynucleotide, a host cell, and a method for producing the polypeptide. Additionally, the claims are directed to an antisense oligonucleotide complementary to a mRNA comprising SEQ ID NO: 1 and an antisense polynucleotide less than about 200 bases in length.

Applicant's arguments (Paper No. 14,21 February 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

CLASP molecules have a similar structure in that they have cadherin EC motifs, putative transmembrane domains, a number of putative ITAM domains and a high degree of sequence similarity. Applicant indicates that the CLASP-1 is the subject of a patent application, currently in allowance. Applicant explains that CLASP-1 plays a pivotal role in cell-cell communication, and is thought to be part of a developmental "switch" that initiates a developmental pathway in response to certain cell-cell interactions. Applicant submits that because CLASP-5 shares a high degree of sequence identity with CLASP-1 and plays a role in cell-cell communication, it has similar utilities to that of CLASP-1. Applicant also states that the role of sequence similarity in determining genetic function cannot be ignored and cites Enright et al. (Nucleic Acids Res 30(7): 1575-1584, 2002).

Applicant's arguments have been fully considered but are not found to be persuasive. The assertion that the disclosed CLASP-5 polynucleotide has biological activities similar to protein family members having a role in cell-cell communication and developmental pathways is not credible in the absence of supporting evidence, because the relevant literature reports numerous examples of polypeptide families wherein individual members have distinct, and even opposite, biological activities. For example, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences

administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598; see Abstract and pp. 1594-1596). Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF-β family members BMP-2 and TGF-β1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). See also Massague, who reviews other members of the TGF-β family (1987, Cell 49:437-8, esp. p. 438, column 1, second full paragraph to the end). Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720; see p. 717, second paragraph of Introduction). Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48).

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional

[illegible] protein and [illegible] occur

because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Enright et al. describe a novel approach for rapid and accurate clustering of protein sequences into families, but state that "the presence of a shared domain within a group of proteins does not necessarily imply that these proteins perform the same biochemical function" (pg 1575, ¶ 2). Thus, the specification fails to support the asserted credible, specific and substantial utility of cell-cell communication activity.

(ii) Applicant asserts that the utility of a gene product may be asserted by its expression pattern. It is noted that Applicant cites Example 12 of the Revised Interim Utility Guidelines Training Materials for emphasis. Applicant also argues that the claimed polynucleotide represents a gene that is differentially expressed in immune system cells. Applicant contends

or manipulating an immune system response. Applicant submits that according to Figure 2A, expression of CLASP-5 is detectable in spleen, placenta, peripheral blood lymphocytes, thymus, and kidney cells. Applicant states that these tissues, with the exception of kidney cells, are well known to be rich in immune system cells. Applicant also argues that CLASP-5 shows strong expression in several human and mouse immune cell lines (see Figure 2B). Applicant asserts that CLASP-5 is highly expressed in MV4-11 cells (B myelomonocyte) , THP cells (B monocyte) , HL60 (B promyelocyte) , and 9D10 cells (murine B cell line), but not Jurkats (T cell line) or 293 cells (human embryonic kidney cells). Applicant concludes that CLASP-5 is associated with T cells as well as B cells.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the asserted patentable utilities of detecting immune system cells, monitoring the development of an immune system cell, or manipulating an immune system response for the claimed CLASP-5 polynucleotide are not substantial because one skilled in the art would not readily use the claimed polynucleotide sequences to make protein to be used for tissue/cell-typing in a real world sense since the protein is not specific to one tissue or cell and is not associated with any disease or disorder. Furthermore, this asserted utility is not specific because numerous unrelated polynucleotide sequences would also show a similar tissue/cell typing pattern. Also, evidence of mere expression in a tissue or cell is not tantamount to a showing of a role in cell-cell communication. Although Figure 2B indicates that CLASP-5 is expressed in MV4-11 cells, THP cells, HL60 cells, and 9D10 cells, the specification does not teach that

cancerous B cells. Additionally, one skilled in the art would not be able to conclude that CLASP-5 is associated with T cells because there is no expression of CLASP-5 in Jurkat cells or 3A9 cells, both T cells.

Furthermore, the fact pattern of Example 12 of the Revised Interim Utility Guidelines Training Materials (particularly pg 69-70) is significantly different from the fact pattern of the instant case. In the Training Materials, if the receptor of Example 12 is found on cell membranes of melanoma cells but not on the cell membranes of normal skin cells, there is credible, specific and substantial asserted utility and a well established utility. However, the examples in the instant application do not indicate that the CLASP-5 polynucleotide or polypeptide have differential cell expression or association with a disease or condition. Therefore, the specification fails to support the asserted credible, specific and substantial utility of cell-cell communication activity.

10. Claims 1-4, 6-15, 30, and 38-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pg 9 of the previous Office Action (Paper No. 12, 14 August 2002).

11. Additionally, claims 1-4, 6-11, 13-15, 30, 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

connected, to make and/or use the invention. The basis for this rejection is set forth for claims 1-4, 6-11, 14-15, and 30 at pg 9-14 of the previous Office Action (Paper No. 12, 14 August 2002).

Applicant's arguments (Paper No. 14,21 February 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that in Figure 6B of the specification, several polymorphisms (i.e. allelic variations) in the CLASP-5 sequence are disclosed. Applicant argues that these polymorphisms lead to 6 single nucleotide variants and 2 alternative splice variants. Applicant states that the instant application explicitly discloses the sequence of at least 8 CLASP-5 variants, which may be present singly or in any combination in the CLASP-5 sequence. Applicant contends that the actual number of permutations of the polymorphisms is 40,320. Applicant concludes that Figure 6B describes over 40,000 possible variants. Applicant submits that the number of variants described in the working examples alone are sufficient for enabling the CLASP-5 variants of the claims.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification not teach the functional characteristics of CLASP-5 or any polynucleotide variants. Additionally, the problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. Certain positions in the amino acid sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of

mutations in E-cadherin that cause familial gastric cancer. For example, the ***single*** nucleotide substitution in the donor splice site of consensus sequence of exon 7 (position 1,008) results in a truncated gene product and diminished E-cadherin expression (abstract; pg 403; Table 2). Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one or ordinary skill in the art to determine, without undue experimentation, the positions in the CLASP-5 protein and DNA which are tolerant to change and the nature and extent of changes that can be made in these positions. One skilled in the art would not be able to recognize a variant of CLASP-5 because the specification of the instant application does not define any *specific* functional characteristics of the human CLASP-5 protein. Additionally, the specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Undue experimentation would be required by the skilled artisan to generate the infinite number of CLASP-5 variants recited in the claims and to screen the same for activity. Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polynucleotides to make biologically active CLASP-5 without resorting to undue experimentation to determine what the specific biological activities of the CLASP-5 polypeptide and all CLASP-5 variants are.

(ii) Applicant asserts that throughout the instant specification, several methods have been

argues that upon review of this figure, one of skill in the art would recognize that the amino acids that are conserved have greater importance for CLASP function than other amino acids. Applicant indicates that that a skilled person would recognize that CLASP-5 amino acids that are conservatively substituted could be predictably interchanged with amino acids of the same type. Applicant also contends that a skilled person, upon seeing motifs in Borroto et al.'s ITAM variants, would make these substitutions with a predictable lack of effect on ITAM motif function, and hence the activity of the CLASP protein would not be affected. Applicant argues that several polymorphisms for other CLASP molecules have been provided and since the various members of the CLASP family are very similar to each other, one of skill in the art would recognize that the polymorphism for other CLASPs may be used as guidance for producing further variants of CLASP-5.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, it cannot be determined from the CLASP protein sequence alignment in Figure 8 how these proteins have been designated as belonging to a family, since the structural similarities are not clear. For example, since many of the boxes encompassing various amino acid regions are not labeled, it is not clear what these regions are (i.e., transmembrane domains). Furthermore, none of the proteins in the CLASP family, except for CLASP-1, have defined functions or any functions in common. Therefore, it is unclear of the function of the CLASP-5 polypeptide encoded by the claimed polynucleotides. Since it is known in the art that many polypeptide families have individual members with distinct, and even opposite, biological

protein function would be unaffected by substitutions, additions, or deletions in CLASP-5 motifs or domains. Certain positions in the amino acid sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. One amino acid change can change the entire structure and function of a protein.

Additionally, according to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed". The specification outlines prophetic procedures for modifying CLASP-5 and screening the variants (see pg 39-40 and pg 65-66). However, this is not adequate guidance, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polynucleotides encoding CLASP-5, and to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding same and the lack of direction/guidance presented in the specification regarding the specific chromosomal locus of the CLASP-5 gene and diseases/disorders associated with the gene, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural

fail to recite particular biological activities and also embrace a broad class of structural fragments and variants and which recite any allelic variant, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

12. Claims 1-4, 6-11, 13-15, 30, 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth for claims 1-4, 6-11, 14-15, and 30 at pg 14-17 of the previous Office Action (Paper No. 12, 14 August 2002).

Applicant's arguments (Paper No. 14, 21 February 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the specification describes a large number of CLASP-5 species in Figure 6B. Applicant indicates that this number of CLASP-5 species represents a representative number of nucleic acids to describe the genus of nucleic acid species recited in the claims. Applicant also submits that the specification provides a structural feature common to all members of the genus. With regard to "hybridization" claims, Applicant argues that Figure 6B shows the hybridization experiments using a portion of SEQ ID NO: 1. Applicant states that Example 9 of the "Synopsis of Application of Written Description Guidelines" describes a similar fact pattern involving a hypothetical nucleic acid and unsequenced nucleic acids that

Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polynucleotides recited in the claims. The description of one CLASP-5 polynucleotide and polypeptide in the specification of the instant application is not a representative number of embodiments to support the description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all mutants, derivatives, variants and fragments having at least 95% or more sequence identity to the polypeptide of SEQ ID NO: 2, at least 20 contiguous amino acids of SEQ ID NO: 2, and at least 50 contiguous nucleotides of SEQ ID NO: 1. Therefore, only an isolated polynucleotide consisting of the nucleotide sequence of SEQ ID NO: 1 and a nucleic acid molecule which encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Furthermore, the broad brush discussion of making or screening for allelic variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only one member, CLASP-5 of SEQ ID NO: 1, was disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

Furthermore, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure,

present in the claims is a partial structure in the form of a recitation of percent identity and polynucleotide/polypeptide fragments. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Additionally, with regard to claim 39, simply reciting hybridization conditions in the claim does not yield adequate written description of the polynucleotides encompassed. The claim encompasses an infinite number of polynucleotides that hybridize to the nucleic acid sequence of SEQ ID NO: 1. These polynucleotides may be structurally and functionally divergent from the polynucleotide of SEQ ID NO: 1. The fact patterns of Example 9 in the "Synopsis" and of claim 39 are significantly different. In Example 9, the nucleic acid molecule encodes a protein with a specific function. In the instant application, the function of the CLASP-5 protein has not been characterized (see enablement above).

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Stringency is relative, and the art does not recognize a single set of conditions as

absence of a recitation of clear hybridization conditions (e.g., hybridizes at wash conditions of

A X SSC and **B** % SDS at **C**°C"), claim 39 fails to define the metes and bounds of the varying structures of polynucleotides recited.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB
Art Unit 1647
April 30, 2003

Elizabeth C Kemmerer

ELIZABETH KEMMERER